



# **Putting Children's Environmental Health in Social Context:**

**Recent Findings from the Columbia Center  
for Children's Environmental Health**

**EPA Science Forum 2004**

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**Washington D.C.**

**Presenter: Virginia A. Rauh, Sc.D.**

**Frederica Perera (Director), Robin Whyatt, Rachel Miller, Pat Kinney,  
Peggy Shepard, David Evans, Howard Andrews**

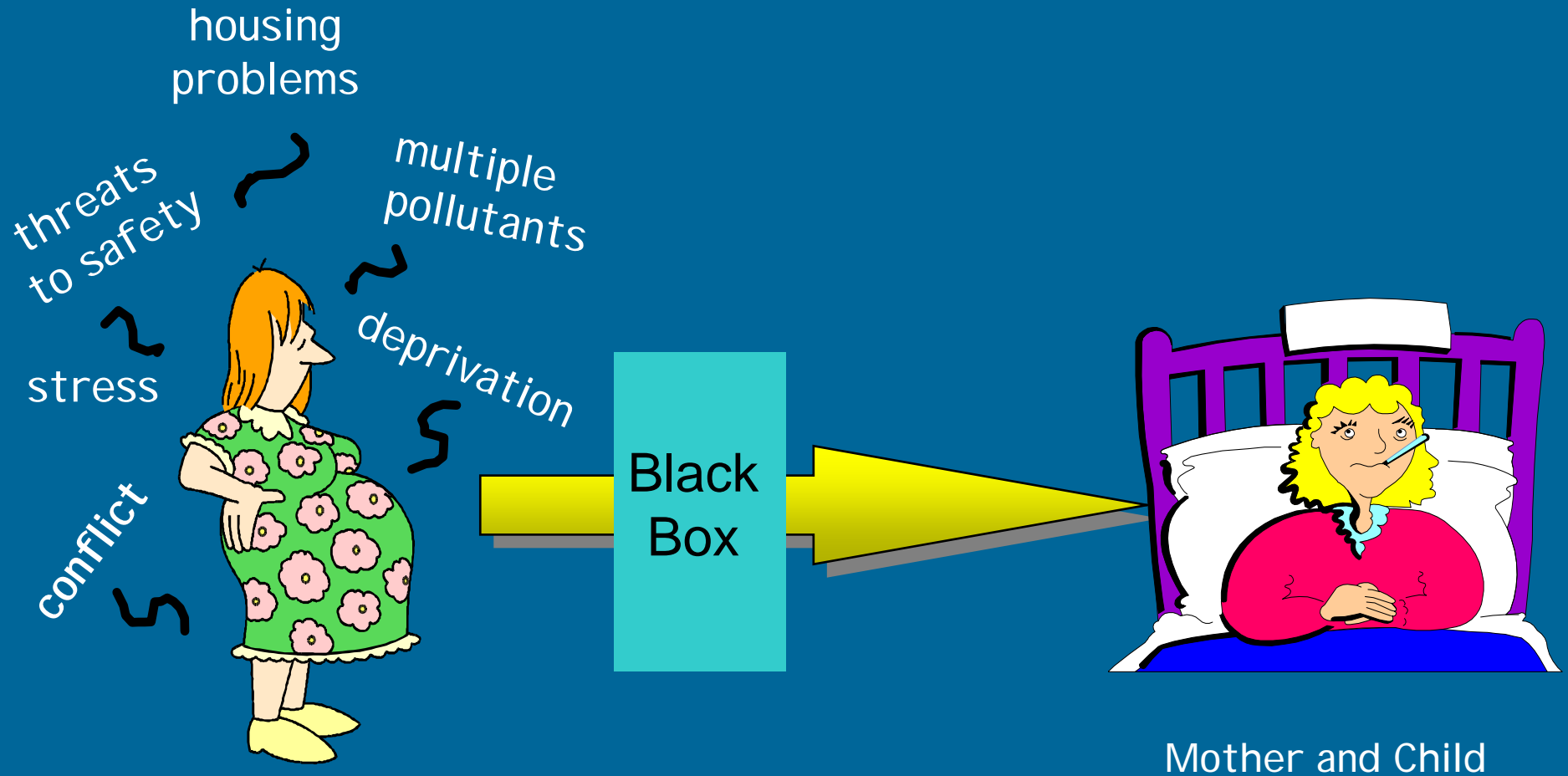
# Columbia Center for Children's Environmental Health



## Mailman School of Public Health

Funded by NIEHS, EPA, and private foundations: 1 RO1 ES08977, 5 P01 ES09600/EPA R827027, R01 ES08977-05A1, EPA Star grants (R-82860901 & R-827027), Bauman, Beldon, EFA, Hansen, Harriman, JMF, NYCT, Rasmussen

# How Do Social and Physical 'Toxicants' Get Under Your Skin?





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### **Exposures:**

Air Pollutants (fossil fuel)

Pesticides

Environmental tobacco  
smoke (ETS)

Allergens

Social stressors

### **Susceptibility:**

Inadequate nutrition

Genetic factors

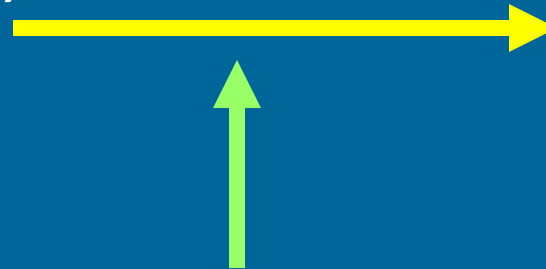
Social stressors

### **Effects:**

Neurodevelopment

Asthma

Cancer risk



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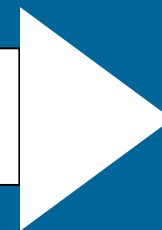
Pregnancy

7-8 years

**Exposure  
Assessment**

**Biomarkers of Exposure  
Effect/Susceptibility**

**Outcome**



### Environmental Exposures

#### Air Pollutants

- PAH, PM
- Pesticides
- ETS

Allergens

Metals

### Biomarkers

PAH-DNA Adducts  
Pesticides  
Cotinine, 4-ABP-Hb

Immune changes

Lead, Mercury

### Clinical Outcomes

Fetal Growth  
Child Neurodevelopment

Persistent Wheeze/Asthma

Cancer Risk

### Susceptibility Factors

- Nutritional deficits
- Social stressors

Vitamins A,C,E



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## **Cohort**

**Number: 730 mother/newborn pairs**

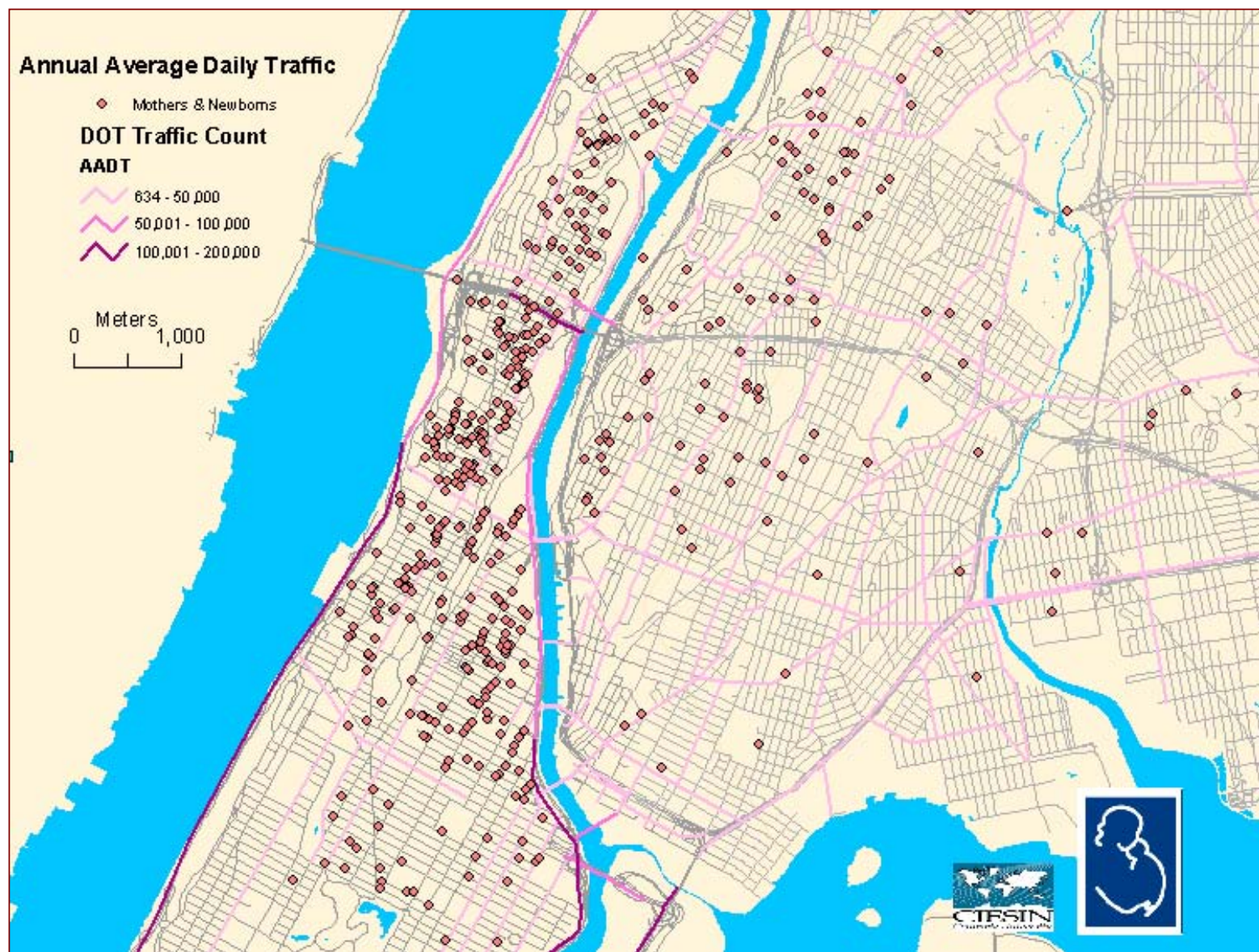
**Ethnicity: African American and Dominican**

**Residence: Northern Manhattan & South Bronx**

**Characteristics:**

- **Non-smokers**
- **Non-illicit drug users**
- **No history of HIV, hypertension, diabetes**

# GIS: Residences of Study Subjects in NYC Cohort Study





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### **Demographics (N=639)**

**Maternal Age** 28.2 ± 5.1

**Ethnicity**

Hispanic 63%

African American 37%

**Medicaid recipient** 90%

**Marital Status**

Never married 67%

**Education**

< High School 35%

**Annual Household Income**

< \$10,000 42%

**Lacked basic necessities**

shelter, food, clothing, heat, medicine 41%





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## **Environmental Measures**

48-hour personal air monitoring  
(begun in 1999)



2-week integrated indoor air  
samples (begun in 2001)





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## **Biologic Samples:**

- Umbilical cord blood
- Maternal blood
- Meconium
- Urine



Medical record data: gestational age, gender, birth weight, length, head circumference, maternal height, pre-pregnancy weight and weight gain, medications



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## **Insecticides measured in environmental and biologic samples**

### **Organophosphates**

Chlorpyrifos

Diazinon

Malathion

Methyl parathion

### **Pyrethroids**

*cis*-Permethrin

*trans*-Permethrin

### **Carbamates**

Bendiocarb

Carbaryl

Carbofuran

Propoxur

## Summary of Key Findings Related to Exposures

- PAH detected in 100% air samples
- PAH-DNA adducts detected in ~40% newborn cord bloods
- Ingestion of dietary PAH was uncommon (4.9%)
- Chlorpyrifos, diazinon, propoxur detected in 100% air samples and 57%-97% of blood samples
- Significant decrease in air and blood levels of chlorpyrifos, diazinon, and propoxur after the EPA reg. action (6/2000)
- Prenatal ETS exposure occurred in 39.1% of the sample; postnatal ETS exposure in the first two years of life occurred in 38.7% of the sample
- One or more material hardships were reported by 37.7% of women during pregnancy (no food, housing, or clothing)



## Relationship between Social Conditions and Chemical Exposures in the New York Cohort

	<u>PAH</u>	<u>ETS</u>	<u>Allergens</u>
Unmarried	ns	p<.05	
Extreme poverty	ns	p<.01	
Teenage mother	ns	p<.01	
Educational level	ns	p<.05	
Total number social stressors	p<.05	p<.01	
Housing Disrepair			p<.01
Floor level of residence	p<.05	ns	
Pregnancy during heating season (Oct.1 – May 31)	p<.001	ns	

Results suggest that socially and physically aversive exposures tend to co-occur, so that analyses of environmental effects must address confounding as well as possible interactions.



## Race/Ethnic Differences in Patterns of Socially Stressful Conditions

	<u>Af. Americans</u>	<u>Dominicans</u>	<u>p -value</u>
Dilapidated Housing*	48.1%	38.7%	<.05
Material Hardships:			
Go without food	7.8%	25.0%	<.001
Go without housing	10.9%	28.7%	<.001
Go without clothing	18.1%	37.6%	<.001
Single parenthood	85.9%	54.7%	<.001

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\*Index of disrepair (holes in ceilings and walls, leaky pipes, water damage, peeling paint)

**These differences exist despite similarities in educational level and income, across communities and ethnic groups**

# Summary of Key Findings Related to Biomarkers Indicate Fetal Exposure and Differential Susceptibility

	Newborns	Mothers	P-value†
Cotinine (ng/ml)	1.67	1.26	<0.001
BP-DNA (10 <sup>8</sup> )	0.22	0.21	0.13
CPF (pg/g)	5.99	5.96	NS

† 230 newborns: 230 mothers difference by paired T-test or Wilcoxon Signed Ranks Test, \*\* p< .001



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## **Three insecticides detected frequently in indoor and maternal personal air and in maternal and newborn blood samples**

**Chlorpyrifos:** 99% of air and 70-71% of blood samples

**Diazinon:** 100% of air and 48-49% of blood samples

**Propoxur:** 100% of air and 40-41% of blood samples

Maternal and newborn blood levels were similar and highly correlated showing that the insecticides were readily transferred from the mother to her unborn child



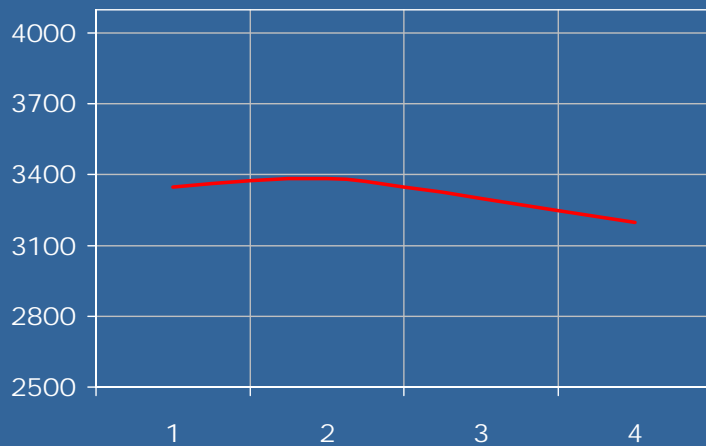


## Summary of Key Findings related to Fetal Outcomes

- Prenatal PAH exposure is associated with decreased birth weight and head circumference among African American infants
- Prenatal chlorpyrifos exposure (a non-persistent pesticide) is associated with decreased birth weight among African Americans and reduced birth length in total sample

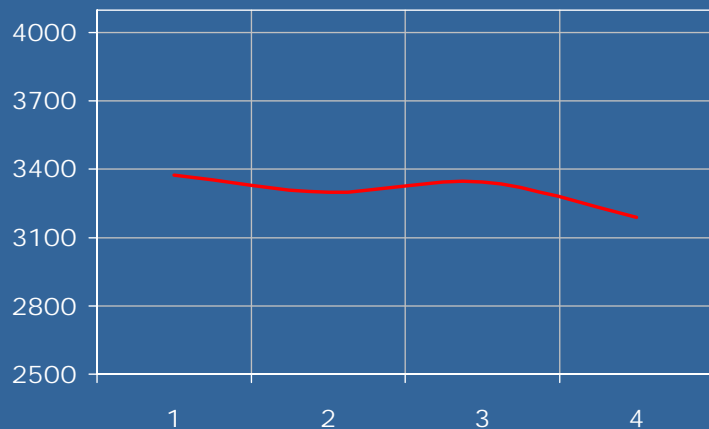


# Birth weight by pesticides in cord plasma



## Chlorpyrifos

150.1 gm lowest vs highest exposure,  $p=0.03$



## Sum chlorpyrifos and diazinon

186.3 gm lowest vs highest exposure,  $p=0.01$

<sup>1</sup>Group 1=below LOD; group 2=lowest 3<sup>rd</sup> > LOD; group 3=middle 3<sup>rd</sup> of > LOD; group 4=highest 3<sup>rd</sup> > > LOD.

*Whyatt et al., in press*



# Implications of Observed Adverse Birth Outcomes for Child Health & Development

**Lower birth weight, even in the normal range, is associated with adverse effects on health and physical and cognitive development**

*Rice and Barone, 2000*

*Matte et al, 2001*

*Richards et al, 2002*

*Dietz, 1994; Barker, 1996*



## **Summary of Findings Related to Respiratory Health: Elevated Asthma Risk by Age 2**

- **31% diagnosed by a physician as having or likely to have asthma**
- **19% visited an emergency room due to breathing problems**
- **High rates of antigen specific- cord blood T cell proliferation and high anti-cockroach and anti-mouse IgE levels at age 2**
- **Interaction between prenatal PAH and postnatal ETS exposure on respiratory outcomes**

*Miller et al., 2003*

# The New York Times

NEW YORK, MONDAY, MARCH 22, 2004

## Babies Are Larger After Ban On 2 Pesticides, Study Finds

By RICHARD PÉREZ-PEÑA

Pregnant women in upper Manhattan who were heavily exposed to two common insecticides had smaller babies than their neighbors, but recent restrictions on the two substances quickly lowered exposure and increased babies' size, according to a study being published today.

The researchers, led by a team from Columbia University, looked at babies born to women living in Harlem and Washington Heights, and divided them into four groups, based on the amounts of the pesticides chlorpyrifos and diazinon found in the mothers' blood and umbilical cord blood. In the group with the highest levels, babies averaged 6.6 ounces lighter and one-third of an inch shorter than those in the group with no measurable amount of the insecticides in the blood.

The authors say that theirs is the first reported study to show a link between umbilical cord levels of these two pesticides and newborn size. They said it was also the first to document an improvement in birth size from curtailing use of a pesticide.

The study was part of a long-running project by Columbia researchers to gauge the effects of urban pollution on mothers and children. Dr. Frederica P. Perera, director of that effort, said the new results are significant because "birth weight is a very good predictor of later health and development of children, including physical development, mental development and school performance."

Chlorpyrifos and diazinon were once found in dozens of over-the-counter products and were heavily used by professional exterminators. The federal Environmental Protection Agency banned them from indoor use in stages, from 2000 to 2002, though both pesticides are still used in agriculture and are commonly found on produce.

The new study of 314 babies, being published in the journal *Environmental Health Perspectives*, found that the ban had a notable effect on pesticide exposure and infants' size.

"It was very marked, and pretty immediate," said Dr. Robin M. Whyatt, the principal author of the study and an assistant professor at the Mailman School of Public Health at Columbia.

Among children born from 1998

to 2000, about one-third fell into the high-exposure group. But of those born in 2001 and 2002, just one out of 77 was in that group, Dr. Whyatt said. As pesticide levels fell, she said, infant size rose.

What made that change all the more remarkable, she said, is that while exposure to the pesticides dropped significantly in 2000, 2001 and 2002, it did not suddenly fall to zero. The E.P.A. began phasing out sales for residential use in 2000, for chlorpyrifos and 2001 for diazinon, and many stores voluntarily took the products off their shelves before they were required to do so.

But the total bans on indoor use did not take effect until the end of 2001 for chlorpyrifos and the end of 2002 for diazinon. Surveys by Columbia found that many stores in minority areas were still selling products with those pesticides as late as

### Gauging the effects of urban pollution on mothers and children.

mid-2003.

"Our data indicate that the exposure levels are still going down," Dr. Whyatt said. "We may continue to see added benefits of this ban over time."

Since 1997, Columbia's environmental health project has measured the effects of smoking, air pollution and other factors on women in upper Manhattan and their children. Dr. Perera said the researchers planned to track the children over many years, as they go through school, to see if exposure to pesticides and other pollutants can be shown to affect mental development and academic performance.

The women who participate, all of them black or of Dominican descent, were recruited from the prenatal clinics at Harlem Hospital and New York-Presbyterian Hospital. In the most recent study of pesticide levels, women were excluded for other factors, like smoking or high exposure to cigarette smoke, that also affect birth weight and could skew the results.

A10 THURSDAY, MARCH 25, 2004

## Birth Weights Up After EPA Pesticide Ban, Study Finds

By MARC KAUFMAN  
Washington Post Staff Writer

A federal ban on two popular household insecticides has significantly reduced the number of underweight babies born in neighborhoods where the chemicals had been widely used, a study has found.

Researchers at Columbia University found that infant birth weights and birth lengths in upper Manhattan improved immediately after the pesticides chlorpyrifos and diazinon, used in a number of household products, were banned for indoor use by the Environmental Protection Agency beginning in 2000.

"We were surprised to see such a significant

association between exposure to the pesticides and birth weight," said principal author Robin M. Whyatt of Columbia's Mailman School of Public Health. "There is no question that this is an instance where regulation worked—that the EPA imposed a ban and there was immediate benefit from it."

The research tested levels of the pesticides in the blood of pregnant women and their infants before and after the ban. The results showed that the infants exposed to the highest amounts of the chemicals in the womb were most likely to have low birth weights, which generally predicts a higher rate of health and developmental problems.

Whyatt said the babies of pregnant women

exposed to the greatest amount of the banned insecticides were on average 6.6 ounces lighter than those of women with lower exposures. She said the difference in birth weight was highly significant, comparable to the gap between pregnant women who smoke and those who do not.

The two pesticides were found in many products to control cockroaches and other insects. They were banned after the EPA found that typical concentrations in homes were above the allowable levels set by the agency. Based on animal studies, the agency had concluded that the pesticides, from the family of chemicals known as organophosphates, could cause low birth weight in infants and devel-

opmental problems for children.

The makers of the products—Syngenta Crop Protection for diazinon and Dow Agro-Sciences for chlorpyrifos—at first opposed the ban but later voluntarily consented to stop selling them for use in households and by exterminators.

The ban did not affect the use of the pesticides for crop protection. According to Agriculture Department statistics, diazinon residues are most commonly found on mushrooms and chlorpyrifos on peaches.

Whyatt said her study did not look at the effects of trace amounts of the pesticides on food, but she did have concerns about exposing migrant workers to the chemicals.

The new study, published in the journal *Environmental Health Perspectives*, followed the birth of 314 babies. It is part of a broader, multi-year research project begun in 1998 that examines the health of pregnant women exposed to air pollutants, tobacco smoking and allergens, as well as pesticides. The project is funded by the National Institutes of Health and the EPA.

Whyatt said researchers found that pregnant women used insect-control products in equal amounts before and after the ban, but the new products did not contain chlorpyrifos or diazinon.

The study focused on women in Harlem and Washington Heights, areas with many poor and minority families. The researchers will continue to follow the children tested at birth to see how exposure to the pesticides affects their development.

# The Washington Post

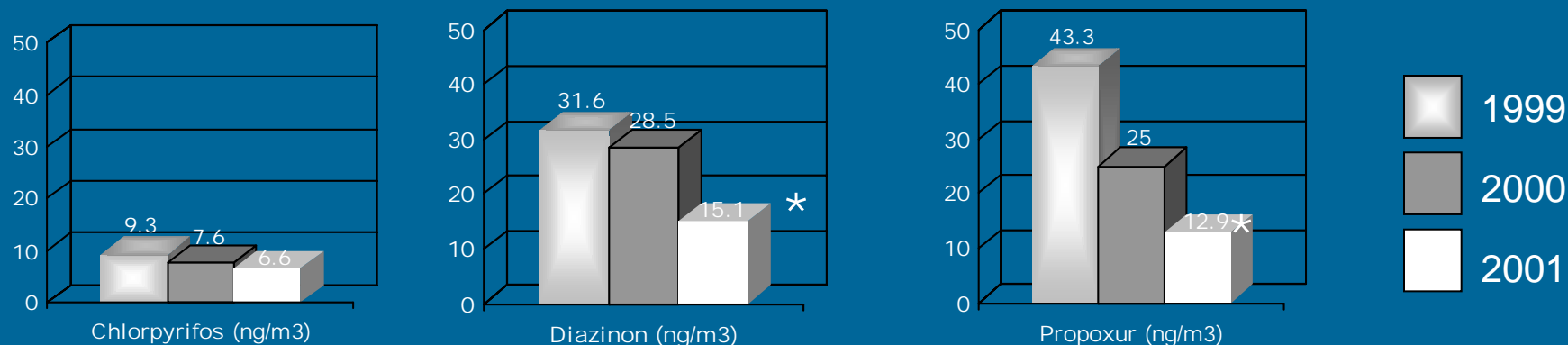
THURSDAY, MARCH 25, 2004

GOVERNMENT

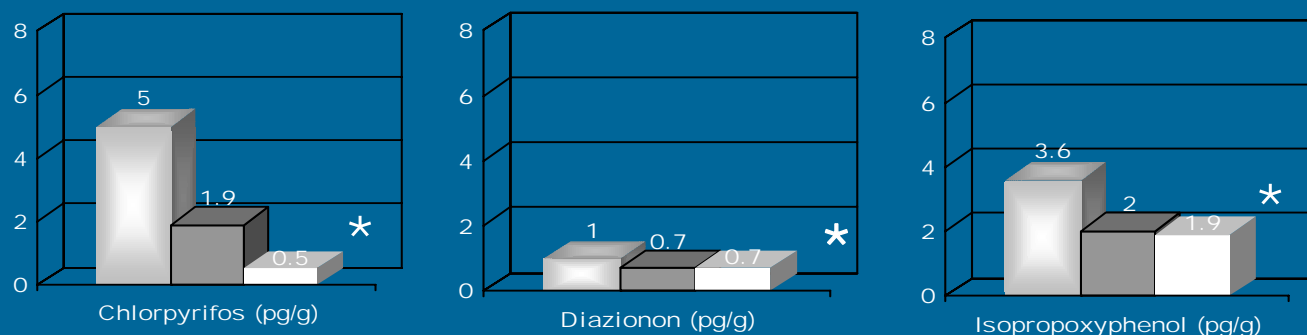
THE WASHINGTON POST

# Geometric mean pesticide levels by year of personal monitoring or year of delivery

## Personal air samples (ng/m<sup>3</sup>)



## Cord blood levels (pg/g)



\* p < 0.05 linearity trend test

*Whyatt et al., EHP, 111: 749-756, 2003*



## Associations between fetal growth and cord blood OP levels by year of delivery

### Birth weight (gm)

### Birth length (cm)

#### Born prior to 1/1/2001

Chlorpyrifos  $B^1 = -67.3, p=0.008$

$B = -0.43, p=0.004$

Sum OP<sup>2</sup>  $B = -68.5, p=0.007$

$B = -0.46, p=0.004$

#### Born after 1/1/2001

Chlorpyrifos  $B = 30.7, p=0.7$

$B = 0.07, p=0.9$

Sum OP  $B = 0.6, p=1.0$

$B = 0.07, p=0.8$

<sup>1</sup>Unit decrease in birth weight and length for each log unit increase in OP

<sup>2</sup>Sum of diazinon and chlorpyrifos adjusted by EPA relative potency factors

Whyatt et al., in press





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## **Intervention study to reduce residential pesticide exposure during pregnancy**

### **Integrated Pest Management**

- Repairing of holes in walls and ceilings
- Repairing of water damage
- Sealing of cracks and crevices
- Extensive cleaning
- Targeted application of pest gels







# Postnatal Assessment

## Timeline



Denver II

X

Fagan Test of  
Infant Intelligence

X

Bayley scale of  
Infant Intelligence

X

X

X

Home Inventory

X

Childhood Behavior  
Checklist

X

Wechsler Pre-School &  
Primary Scale of Intelligence

X

X

Respiratory health/asthma –Interview every 3 mo., lung function 60 mos.



## Developmental Outcomes: Bayley Scales

			% Delayed	
	<u>Mean</u>	<u>SD</u>	<u>Mild</u>	<u>Moderate</u>
12-month: (n=313)				
Mental Development	93.77	9.71	16.0 %	1.0 %
Motor Development	96.41	12.65	15.4%	1.6%
24-month: (n=193)				
Mental Development	84.16	12.61	39.4%	11.9%
Motor Development	97.36	12.11	12.0%	2.6%
36-month: (n=92)				
Mental Development	85.78	11.94	38.3%	9.6%
Motor Development	97.85	14.63	13.8%	6.4%



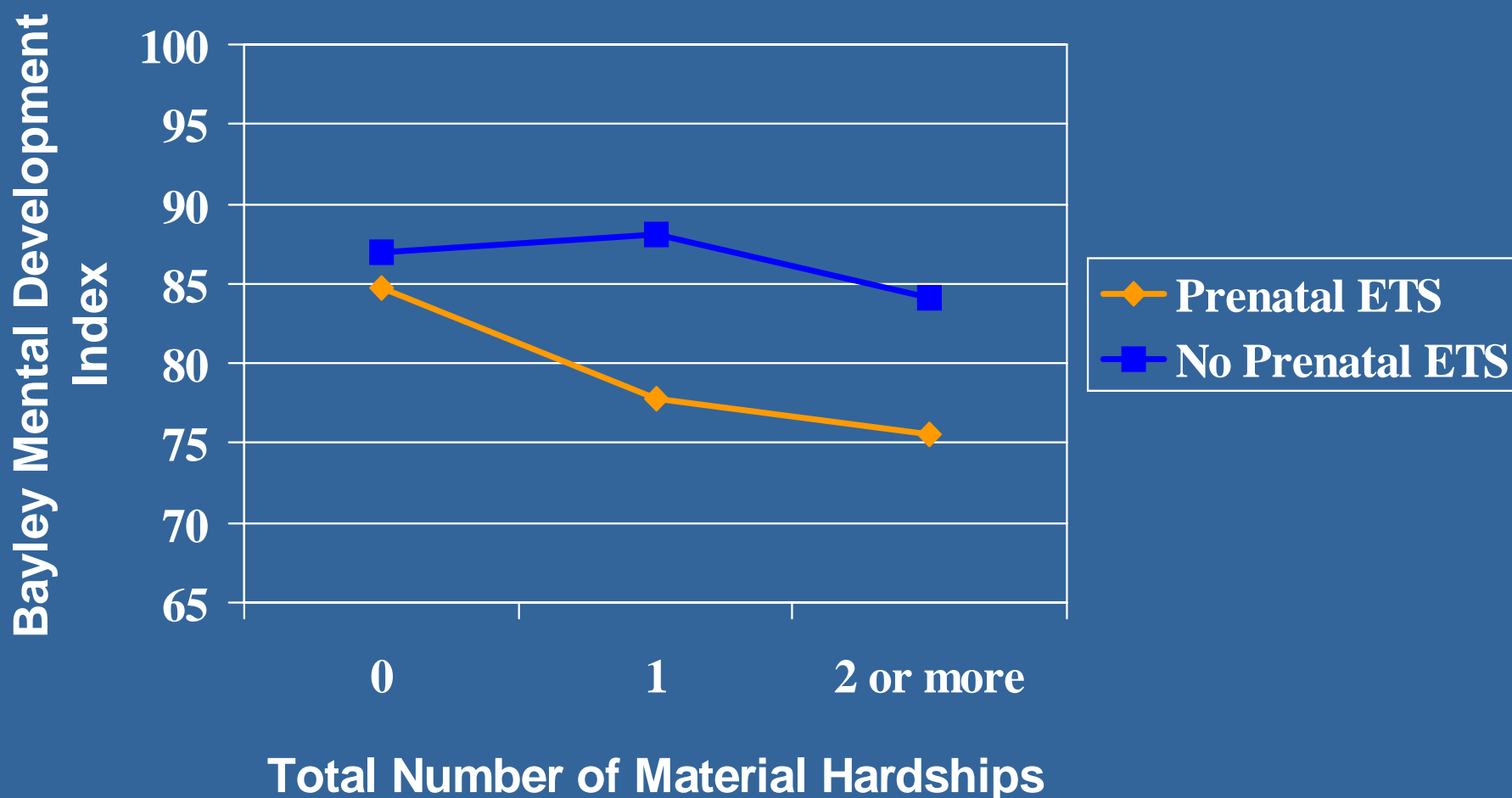
## **Developmental Delays in the Cohort (by 24 mo)**

**The Bayley test at 24 mo is highly predictive of children's later cognitive abilities:**

- **17% of children classified as mildly or moderately delayed (12 mo)**
- **41% classified as mildly or moderately delayed (24 mo)**



## Regression<sup>a</sup> of 24-month Cognitive Development on Prenatal ETS Exposure, by Level of Material Hardship



<sup>a</sup>Adjusted for race/ethnicity, gender, gestational age at delivery, age at testing, marital status, maternal age, PAH exposure, and postnatal ETS

## Summary of Results Related to Secondhand Smoke

1. Prenatal residential ETS exposure was associated with a 5-point adjusted mean decrement in 24-month cognitive development score (Bayley MDI) in a low-income minority sample
2. This 5-point mean decrement resulted in a two-fold risk of developmental delay ( $< 80$ ) on the Bayley MDI
3. Joint exposure to prenatal ETS in the context of chronic material hardship (unmet basic needs) was associated with a 7-point decrement in 24-month MDI, suggesting that the neurotoxic effects of ETS are exacerbated under conditions of deprivation
4. The main effect of ETS was observed for prenatal and not postnatal exposure

## Possible Mechanisms for Main ETS Effect

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- Alteration of receptor-mediated cell signaling in the brain (e.g., Slotkin, 1998)
- Anti-estrogenic effects (e.g., Bui et al., 1986)
- Induction of P450 enzymes (e.g., Manchester et al., 1987)
- DNA damage resulting in the activation of apoptotic pathways (Nicol et al., 1995; Wood and Youle, 1995), and/or agents that bind to receptors for placental growth factors resulting in decreased exchange of oxygen and nutrients (e.g., Dejmek et al., 2000)



# Comparability of Results

## Main ETS Effect:

- ETS effect is smaller than reported active prenatal smoking effects (Makin et al., 1991; Weitzman et al., 2002)
- ETS effect is comparable to the cognitive effects of prenatal low-level lead exposure in the preschool years, with cognitive effect sizes ranging from 3.4-6.6 points (e.g., Schwartz, 1994)
- Children with MDI scores below 80 are at increased risk for performance deficits in language, reading, and math in the early school years



# Possible Interpretation of Results

## Interaction of ETS and Material Hardship:

- Material hardship may be a marker for exposure to other unmeasured toxicants with possible synergistic effects (Mattson et al., 2002; Eyler et al., 1998)
- Individuals exposed to both ETS and material hardship may have a third risk factor in common with a direct adverse impact on development: dietary deficiency (Rogers et al., 1998)

# Possible Interpretation of Results

## Interaction of ETS and Material Hardship:

- The ETS-material hardship interaction is comparable to lead-SES interaction effects (e.g., Weiss, 2000) or cocaine-SES interaction effects (Eyler et al., 1998)
- The interaction suggests a stress mechanism by which the prenatal toxicant exposure affects arousal regulatory mechanisms, resulting in the child's vulnerability to socially stressful environments (Mayes, 2002 )
- Adaptation to a challenge may depend upon the child's threshold for activation of the catecholamine and norepinephrin arousal system, and this threshold may be impaired by the prenatal toxicant exposure. Some evidence from the animal literature is relevant (Gauda et al., 2001; Meaney et al., 2002; McEwen, 1998).



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## **Conclusions (I)**

- **100% of babies prenatally exposed to multiple neurotoxicants**
- **Heightened fetal susceptibility to PAH--DNA damage (on the order of 10-fold)**
- **Adverse effects of prenatal PAH, pesticides, and ETS on birth outcomes**
- **Direct benefits of CPF regulation on fetal development**



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## **Conclusions (II)**

- **Interaction between PAH-DNA adducts and ETS on fetal growth**
- **Prenatal ETS associated with adverse effects on cognitive development**
- **Interaction between prenatal ETS and social adversity on cognitive development**
- **Developmental, procarcinogenic, and respiratory effects exerted by same pollutant**

## **Environmental exposures and social context:**

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- **Environmental pollutants are disproportionately distributed in society**
- **Pollutants rarely occur in isolation, so that environmental risk is often cumulative**
- **Processes thought to link social conditions and health frequently involve adverse health behaviors such as smoking, alcohol, poor dietary practices and other toxic exposures**

## Environmental exposures and social context (cont.):

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- Social and physically toxic exposures are both ‘stressful’, sharing common biological pathways involving neuroendocrine and immune system functioning
- Emerging evidence that physically toxic exposures interact with social adversity to exacerbate illness



## Future Directions

- Expand size of cohort to 740 mother and child pairs in order to follow children through age 7-8
- Incorporate additional biomarkers using genomics and proteomics
- Incorporate additional biologic measures of response to psychosocial stress
- Parallel laboratory-based research to Identify mechanisms
- Translate research findings into new prevention initiatives in education and policy



## Issues for Future Environmental Research in Social Context

- How do we operationalize social adversity so that it is meaningful across populations?
- What are the biological mechanisms that translate social adversity into health and developmental problems?
- What are biomarkers of social stress (cortisol, etc.)?
- How does social adversity work to moderate the impact of chemical toxicants?
- Might social context act to turn on or off certain genes?
- What types of longitudinal models are appropriate for disentangling prenatal from cumulative postnatal effects as children develop? Issue for the NCS?



## Centers for Children's Environmental Health: Summary of Cohort Studies

	Illinois	Berkeley	Columbia	Mt. Sinai	Cincinnati
Study Design	Pre-pregnancy / Pregnancy Cohort	Pregnancy / Birth Cohort	Pregnancy / Birth Cohort	Pregnancy / Birth Cohort	Pregnancy / Birth Cohort
Number of Subjects Enrolled	164 couples <sup>a</sup> goal=400	601 women	556 women <sup>a</sup> goal=730	479 women	130 women <sup>a</sup> goal=400
Characterization of the Population	Hmong and Laotian couples of childbearing age	Low-income Mexican and Mexican-American women in agricultural community	Dominican and African-American women	Public and private prenatal patients	Public and private prenatal patients
Location	Green Bay and Appleton, WI	Salinas Valley, CA	New York City (Harlem, South Bronx, Washington Heights)	New York City (East Harlem)	Cincinnati, OH
Major exposures	PCBs <sup>b</sup> , Methylmercury	Pesticides, allergens, metals	PM <sup>b</sup> , DEP <sup>b</sup> , PAH <sup>b</sup> , ETS <sup>b</sup> (cotinine), pesticides, allergens, metals	Pesticides, PCBs <sup>b</sup> , metals	Metals, PCBs <sup>b</sup> , pesticides, tobacco smoke (cotinine), alcohol
Major outcomes	Growth, development, behavior, hearing	Growth, development, behavior, asthma, respiratory disease, biomarkers	Growth, development, behavior, asthma, respiratory disease, biomarkers	Growth, development, behavior, biomarkers	Growth, development, behavior, asthma/respiratory disease, hearing

## Contact Points/Assessments

	Illinois	Berkeley	Columbia	Mt. Sinai	Cincinnati
Questionnaire	Enrollment, every two months before pregnancy, monthly during pregnancy, delivery, child aged 6, 9, 12 mos	Pregnancy (enrollment – M=13 weeks, 3 <sup>rd</sup> trimester), delivery (mother and father), child aged 6, 12, 24, 42 <sup>a</sup> , 60 <sup>a</sup> , 84 <sup>a</sup> mos	Pregnancy (3 <sup>rd</sup> trimester), child aged 6, 12, 24, 36, 60, 72 <sup>a</sup> , 84 <sup>a</sup> mos	Pregnancy (3 <sup>rd</sup> trimester), 12, 24, 48 <sup>a</sup> , 72 <sup>a</sup> , 84 <sup>a</sup> mos	Pregnancy (enrollment – M=20 weeks), child aged 1, 12, 24 months; injury questionnaires every 3 mos
Home Walkthrough		Pregnancy, 6, 12, 24, 42 <sup>a</sup> , 60 <sup>a</sup> mos	Pregnancy, 12, 36, 60 mos		Pregnancy, 12, 24 mos
Development Assessment	Birth, 6, 9, 12 mos	Birth, 6, 12, 24, 42 <sup>a</sup> , 60 <sup>a</sup> mos	6, 12, 24, 36, 60, 84 <sup>a</sup> mos	12, 24, 48 <sup>a</sup> , 72 <sup>a</sup> , 84 <sup>a</sup> mos	Birth, 4 weeks, 12, 24 mos
School Evaluation		84 <sup>a</sup> mos	96 <sup>a</sup> mos		
Growth Assessment	Birth, 6, 9, 12 mos	Birth, 6, 12, 24, 42 <sup>a</sup> , 60 <sup>a</sup> mos	Birth, 6, 12, 24, 36, 60 mos	Birth, 12, 24, 48 <sup>a</sup> , 72 <sup>a</sup> , 84 <sup>a</sup> mos	Birth, 4 weeks, 12, 24 mos
Respiratory Assessment		6, 12, 24, 42 <sup>a</sup> , 60 <sup>a</sup> , 84 <sup>a</sup> mos (by questionnaire). Spirometry at 60 mos.	Every 3 mos from birth to 24 mos; every 6 mos from 24 to 60 and to 84 <sup>a</sup> mos (questionnaire). Spirometry at 60 mos.		
Incentives	\$20-35 gift certificates per pre-pregnancy and pregnancy visits. Tee shirts, water bottles, fish measuring tapes, back-to-school packets. gift baskets with baby t-shirts, socks, bottles. Fishing supplies raffles.	\$20-60 in grocery coupons per visit Car seat/stroller Hats, t-shirts, tote bags, toys Raffle after 24 and 84 <sup>a</sup> mos	\$50-300 in cash per visit Educational toy	\$50 in cash per visit Toy	\$25-100 in gift certificates per visit. Tote bags, t-shirts, baby blankets, age-appropriate books